Clinical trial results:
A LONG-TERM, OPEN-LABEL STUDY TO EVALUATE THE SAFETY, PHARMACODYNAMICS, AND EFFICACY OF MIGALASTAT IN SUBJECTS > 12 YEARS OF AGE WITH FABRY DISEASE AND AMENABLE GLA VARIANTS

Summary

EudraCT number	2019-000222-21
Trial protocol	GB
Global end of trial date	29 November 2024

Results information

Result version number	v1 (current)
This version publication date	06 June 2025
First version publication date	06 June 2025

Trial information

Trial identification

Sponsor protocol code	AT1001-036

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04049760
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amicus Therapeutics UK Limited
Sponsor organisation address	One Globeside, Fieldhouse Lane, Marlow, United Kingdom,
Public contact	Patient Advocacy, Amicus Therapeutics, Inc., 001 609662-2000, clinicaltrials@amicusrx.com
Scientific contact	Patient Advocacy, Amicus Therapeutics, Inc., 001 609662-2000, clinicaltrials@amicusrx.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 April 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 November 2024
Global end of trial reached?	Yes
Global end of trial date	29 November 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the long-term safety of migalastat treatment in adolescent subjects diagnosed with Fabry disease who had variants in the gene encoding α-galactosidase A (α-Gal A) (GLA) amenable to treatment with migalastat

Protection of trial subjects:

Subjects enrolled in this study following the completion of migalastat Study AT1001-020. Enrollment into Study AT1001-036 immediately followed the completion of Study AT1001-020 in order to maintain continuity of treatment. Efficacy and safety assessments planned and performed in this study were standard, widely used and generally recognized as reliable, accurate, and relevant.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 October 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 12
Worldwide total number of subjects	16
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	16
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects enrolled into this long-term open-label extension study immediately following the completion of Study AT1001-020. Subjects continued in Study AT1001-036 until eligible to receive reimbursed commercial product in the participating subject's country.

Pre-assignment period milestones

Number of subjects started	16
Number of subjects completed	16

Period 1

Period 1 title	Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Migalastat

Arm description:

migalastat HCl 150 mg QOD

Arm type	Experimental
Investigational medicinal product name	Migalastat HCl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

migalastat HCl 150 mg once every other day (QOD)

Number of subjects in period 1	Migalastat
Started	16
Completed	15
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	Migalastat
Reporting group description: migalastat HCl 150 mg QOD	

Reporting group values	Migalastat	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Adolescents (12- < 18 years)	16	16	
Age continuous Units: years			
arithmetic mean	15.3		
standard deviation	± 1.49	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	10	10	
Prior Enzyme Replacement Therapy (ERT) Status Units: Subjects			
ERT naive	8	8	
ERT experienced	8	8	
Years since Diagnosis of Fabry disease Units: Years			
arithmetic mean	10.79		
standard deviation	± 4.104	-	

End points

End points reporting groups

Reporting group title	Migalastat
Reporting group description: migalastat HCl 150 mg QOD	

Primary: Incidence of Treatment-emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and Adverse Events (AEs) Leading to Discontinuation of Study Drug

End point title	Incidence of Treatment-emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and Adverse Events (AEs) Leading to Discontinuation of Study Drug[1]
End point description: Number of subjects with TEAE, SAE, and AE leading to discontinuation during the study period	
End point type	Primary
End point timeframe: Entire study	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses performed on safety data in this open-label long-term extension study

End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Number of subjects				
Subjects with TEAEs	13			
Subjects with SAEs	1			
Subjects with AE leading to discontinuation	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Month 24 in estimated glomerular filtration rate (eGFR)

End point title	Change from baseline to Month 24 in estimated glomerular filtration rate (eGFR)
End point description: Estimated GFR was calculated using the modified Schwartz formula according to the standards of the central laboratory.	
End point type	Secondary
End point timeframe: Baseline, Month 24	

End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	8[2]			
Units: mL/min x 1.73 m2				
arithmetic mean (standard deviation)	-27.6 (± 8.88)			

Notes:

[2] - 8 subjects had eGFR calculated at Month 24 visit

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Month 24 in urine protein

End point title	Change from baseline to Month 24 in urine protein

End point description:

Renal function was assessed by urine protein levels (mg/L). Urine samples were collected as part of urinalysis.

End point type	Secondary

End point timeframe:

Baseline, Month 24

End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	7[3]			
Units: mg/L				
arithmetic mean (standard deviation)	38.6 (± 79.03)			

Notes:

[3] - 7 subjects had urine protein result at Month 24

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Month 24 in urine albumin

End point title	Change from baseline to Month 24 in urine albumin

End point description:

Renal function was assessed by urine albumin levels (mg/L). Urine samples were collected as part of urinalysis.

End point type	Secondary

End point timeframe:

Baseline, Month 24

End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	6[4]			
Units: mg/L				
arithmetic mean (standard deviation)	-12.7 (± 21.73)			

Notes:

[4] - 6 subjects had urine albumin result at Month 24

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Month 24 in left ventricular mass index (LVMi)

End point title	Change from baseline to Month 24 in left ventricular mass index (LVMi)

End point description:

LVMi was assessed as a measure of cardiac impairment in the study participants. LVMi values for both M-mode and 2D-mode views are presented.

End point type	Secondary

End point timeframe:

Baseline, Month 24

End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	8[5]			
Units: g/m2				
arithmetic mean (standard deviation)				
2D-mode View	4.75 (± 16.679)			
M-mode view	6.01 (± 9.014)			

Notes:

[5] - 8 subjects had LVMi results at Month 24

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Month 24 in Pediatric Quality of Life (PedsQL) scores

End point title	Change from baseline to Month 24 in Pediatric Quality of Life (PedsQL) scores

End point description:

The Pediatric Quality of Life Inventory (PedsQL) was a modular approach to measuring health-related quality of life in healthy children and adolescents and those with acute and chronic health conditions. All components of the PedsQL were scored based on a scale of 0 (never) to 4 (almost always) and linearly

transformed to a 0 to 100 scale as follows: 0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0. Psychosocial, physical, and total scores were calculated based on the response to the questions within the patient reported outcome. The psychosocial score for the PedsQL encompassed 15 questions relating to the subjects' feelings, social interaction with others, and school. The physical score was derived from answers to 8 questions about the subjects' ease of managing physical activity. Total scores were the sum of all the item scores over the number of items answered on all the scales. Change from baseline values of < 0 represents worsening, 0 equals no change, and > 0 represents improvement.

End point type	Secondary

End point timeframe:

Baseline, Month 24

End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	8[6]			
Units: score on a scale				
median (full range (min-max))				
Psychosocial Score	0 (-10 to 28)			
Physical Score	0 (-19 to 19)			
Total Score	-1.1 (-9 to 25)			

Notes:

[6] - 8 subjects had PedsQL results at Month 24

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Month 24 in Fabry-specific Health and Pain Questionnaire (FPHPQ) Score for Pain Intensity

End point title	Change from baseline to Month 24 in Fabry-specific Health and Pain Questionnaire (FPHPQ) Score for Pain Intensity

End point description:

The Fabry-specific Pediatric Health and Pain Questionnaire (FPHPQ) included questions about Fabry disease-specific symptoms. The assessment of "How bad is your pain today?" was measured on a 10-point scale from 0 (no pain) to 10 (pain as bad as you can imagine). A decrease from baseline indicates an improvement in the condition.

End point type	Secondary

End point timeframe:

Baseline, Month 24

End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	8[7]			
Units: units on a scale				
arithmetic mean (standard deviation)	-1.3 (± 3.20)			

Notes:

[7] - 8 subjects completed the FPHPQ pain assessment at Month 24

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Experienced Sudden Onset of Pain As Assessed Using the Fabry-specific Health and Pain Questionnaire (FPHPQ)

End point title	Number of Subjects Who Experienced Sudden Onset of Pain As Assessed Using the Fabry-specific Health and Pain Questionnaire (FPHPQ)

End point description:

Subjects were asked "In the last 3 months how many times did you experience sudden onset of pain?" and responses were reported in the FPHPQ. Responses were categorized as 0, 1 to 3, 4 to 6, and > 6 occurrences of sudden onset of pain.

End point type	Secondary

End point timeframe:

Month 24

End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	8[8]			
Units: Subjects				
0 occurrences	3			
1 to 3 occurrences	4			
4 to 6 occurrences	0			
>6 occurrences	1			

Notes:

[8] - 8 subjects reported frequency of sudden onset of pain on FPHPQ at Month 24

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Month 24 in plasma levels of lyso-Gb3

End point title	Change from baseline to Month 24 in plasma levels of lyso-Gb3

End point description:

Blood samples were collected for measurement of lyso-Gb3 levels in plasma. Plasma levels of lyso-Gb3 were measured using a validated liquid chromatography-mass spectrometry assay.

End point type	Secondary

End point timeframe:

Baseline, Month 24

End point values	Migalastat			
Subject group type	Reporting group			
Number of subjects analysed	8[9]			
Units: ng/mL				
arithmetic mean (standard deviation)	0.05 (± 1.127)			

Notes:

[9] - 8 subjects had lyso-Gb3 result at Month 24

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment period	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups	
Reporting group title	Migalastat

Reporting group description: -

Serious adverse events	Migalastat		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Migalastat		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 16 (81.25%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
skin papilloma			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Vascular disorders			
Raynaud's phenomenon			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
General disorders and administration			

site conditions			
asthenia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
fatigue			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
pyrexia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
cough			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
rhinorrhoea			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Investigations			
aspartate aminotransferase increased			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
blood bilirubin increased			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
alanine aminotransferase increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
blood alkaline phosphatase increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
electrocardiogram T wave biphasic			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

left ventricular mass index subjects affected / exposed occurrences (all) weight increased subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		
Injury, poisoning and procedural complications contusion subjects affected / exposed occurrences (all) road traffic accident subjects affected / exposed occurrences (all) skin laceration subjects affected / exposed occurrences (all) vaccination complication subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		
Cardiac disorders atrioventricular block first degree subjects affected / exposed occurrences (all) left ventricular hypertrophy subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		
Nervous system disorders dizziness subjects affected / exposed occurrences (all) paraesthesia subjects affected / exposed occurrences (all)	 3 / 16 (18.75%) 3 2 / 16 (12.50%) 2		
Gastrointestinal disorders diarrhoea			

subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
abdominal pain upper			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
haematemesis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
impaired gastric emptying			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
tooth impacted			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
toothache			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
vomiting			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hepatobiliary disorders			
hepatic steatosis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
acne			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
dermatitis contact			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
ingrowing nail			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Renal and urinary disorders			

haematuria			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
pollakiuria			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
renal pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
back pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Infections and infestations			
COVID-19			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	6		
nasopharyngitis			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
acute sinusitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
anal abscess			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
bronchitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
ear infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
influenza			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
laryngitis			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
paronychia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
pharyngitis streptococcal			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
sinusitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	4		
Metabolism and nutrition disorders			
decreased appetite			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
obesity			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 June 2019	• References to the Screening Visit were corrected to Baseline Visit since the extension study utilizes the last visit of a feeder study as baseline without the need for re-screening subjects. • New text introduced to cover the contingency of a weight decrease below the requirement for the study treatment dose. • Use of concomitant medications removed as a safety criterion. • A Data Monitoring Committee was considered to be unnecessary in light of the safety profile of migalastat. • Clarification of definitions for non-reproductive potential and acceptable birth control methods. • Deletion of FPHPQ and PedsQL collection at Month 1 visit since that time point was conducted via telephone contact.
19 August 2021	• Visit schedule changed from every 3 months to every 6 months, with intervening telephone contact every 3 months. • Removal of brief physical examinations from assessments to be performed due to change in visit schedule.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported